DEPARTMENT OF HEALTH AND HUMAN SERVICES

TELECONFERENCE MEMORANDUM

Public Health Service
Food and Drug Administration
Center for Biologics Evaluation and Research

Date\Time: March 15, 2007

CBER Representatives: Malcolm Moos, Rafat Husain, Keith Wonnacott

Sponsor's Representative: Stephen Apone, Sr. Scientist I
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STN : 125197/0

Subject: Product Questions

Discussion:

The sponsor was contacted to discuss the following review issues:

1. Validation of the (b)(4) method for sterility testing.
2. (b)(4) lifetime validation; small scale vs. manufacturing scale data
3. Process intermediate hold times; small scale vs. manufacturing scale data
4. Upper and lower limits for certain process controls
5. Acceptance criteria for (b)(4).

With respect to issue 1, there was confusion on the part of the sponsor, in that the BLA referred to use of this test, but teleconference participants did not seem to be aware of this. FDA asked for clarification on this point, and also observed that the compendial tests for sterility would be perfectly acceptable.

The sponsor agreed to provide clarification regarding details of the validations, and to propose limits that were within, rather than at the edge of existing data from the validation studies (items 2 and 3).

The sponsor agreed to propose limits for the steps affected.

The sponsor agreed to consider our discussion of the possibility that (b)(4) might lead to some (b)(4) and to provide a response (note: the in-process and release testing methods in the BLA would identify such problems with high sensitivity and fail lots where (b)(4) became problematic, so this suggestion is considered advisory, rather than a regulatory requirement.)

The sponsor indicated that a response would be provided and discussed as needed. This was done on March 26, 2007, and the points discussed were addressed adequately, with the exception of an upper limit for protein concentration. All of these considerations have been addressed in the review, and letter comments provided where appropriate.

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